

# PATENT COOPERATION TREATY

From the INTERNATIONAL SEARCHING AUTHORITY

# PCT

To:

ERIC POTTER CLARKSON  
Attn. Pilkington, Stephanie  
Park View House  
58 The Ropewalk  
Nottingham NG1 5DD  
UNITED KINGDOM

14 MAR 2005

NOTIFICATION OF TRANSMITTAL OF  
THE INTERNATIONAL SEARCH REPORT AND  
THE WRITTEN OPINION OF THE INTERNATIONAL  
SEARCHING AUTHORITY, OR THE DECLARATION

(PCT Rule 44.1)

Applicant's or agent's file reference MEDY/P31555PC	Date of mailing (day/month/year) 14/03/2005
International application No. PCT/GB2004/004060	FOR FURTHER ACTION See paragraphs 1 and 4 below
International filing date (day/month/year) 27/09/2004	
Applicant MEDICAL RESEARCH COUNCIL	

1. ☒ The applicant is hereby notified that the international search report and the written opinion of the International Searching Authority have been established and are transmitted herewith.

**Filing of amendments and statement under Article 19:**

The applicant is entitled, if he so wishes, to amend the claims of the International Application (see Rule 46):

**When?** The time limit for filing such amendments is normally 2 months from the date of transmittal of the International Search Report; however, for more details, see the notes on the accompanying sheet.

**Where?** Directly to the International Bureau of WIPO, 34 chemin des Colombettes  
1211 Geneva 20, Switzerland, Facsimile No.: (41-22) 740.14.35

**For more detailed instructions,** see the notes on the accompanying sheet.

2. ☐ The applicant is hereby notified that no international search report will be established and that the declaration under Article 17(2)(a) to that effect and the written opinion of the International Searching Authority are transmitted herewith.
3. ☐ **With regard to the protest** against payment of (an) additional fee(s) under Rule 40.2, the applicant is notified that:

- ☐ the protest together with the decision thereon has been transmitted to the International Bureau together with the applicant's request to forward the texts of both the protest and the decision thereon to the designated Offices.
- ☐ no decision has been made yet on the protest; the applicant will be notified as soon as a decision is made.

**4. Reminders**

Shortly after the expiration of **18 months** from the priority date, the international application will be published by the International Bureau. If the applicant wishes to avoid or postpone publication, a notice of withdrawal of the international application, or of the priority claim, must reach the International Bureau as provided in Rules 90bis.1 and 90bis.3, respectively, before the completion of the technical preparations for international publication.

The applicant may submit comments on an informal basis on the written opinion of the International Searching Authority to the International Bureau. The International Bureau will send a copy of such comments to all designated Offices unless an international preliminary examination report has been or is to be established. These comments would also be made available to the public but not before the expiration of 30 months from the priority date.

Within **19 months** from the priority date, but only in respect of some designated Offices, a demand for international preliminary examination must be filed if the applicant wishes to postpone the entry into the national phase until **30 months** from the priority date (in some Offices even later); otherwise, the applicant must, **within 20 months** from the priority date, perform the prescribed acts for entry into the national phase before those designated Offices.

In respect of other designated Offices, the time limit of **30 months** (or later) will apply even if no demand is filed within 19 months.

See the Annex to Form PCT/IB/301 and, for details about the applicable time limits, Office by Office, see the *PCT Applicant's Guide*, Volume II, National Chapters and the WIPO Internet site.

Name and mailing address of the International Searching Authority



European Patent Office, P.B. 5818 Patentlaan 2  
NL-2280 HV Rijswijk  
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Authorized officer

Barbara Klaver

## NOTES TO FORM PCT/ISA/220

These Notes are intended to give the basic instructions concerning the filing of amendments under article 19. The Notes are based on the requirements of the Patent Cooperation Treaty, the Regulations and the Administrative Instructions under that Treaty. In case of discrepancy between these Notes and those requirements, the latter are applicable. For more detailed information, see also the PCT Applicant's Guide, a publication of WIPO.

In these Notes, "Article", "Rule", and "Section" refer to the provisions of the PCT, the PCT Regulations and the PCT Administrative Instructions respectively.

### INSTRUCTIONS CONCERNING AMENDMENTS UNDER ARTICLE 19

The applicant has, after having received the international search report, one opportunity to amend the claims of the international application. It should however be emphasized that, since all parts of the international application (claims, description and drawings) may be amended during the international preliminary examination procedure, there is usually no need to file amendments of the claims under Article 19 except where, e.g. the applicant wants the latter to be published for the purposes of provisional protection or has another reason for amending the claims before international publication. Furthermore, it should be emphasized that provisional protection is available in some States only.

#### What parts of the international application may be amended?

Under Article 19, only the claims may be amended.

During the international phase, the claims may also be amended (or further amended) under Article 34 before the International Preliminary Examining Authority. The description and drawings may only be amended under Article 34 before the International Examining Authority.

Upon entry into the national phase, all parts of the international application may be amended under Article 28 or, where applicable, Article 41.

#### When?

Within 2 months from the date of transmittal of the international search report or 16 months from the priority date, whichever time limit expires later. It should be noted, however, that the amendments will be considered as having been received on time if they are received by the International Bureau after the expiration of the applicable time limit but before the completion of the technical preparations for international publication (Rule 46.1).

#### Where not to file the amendments?

The amendments may only be filed with the International Bureau and not with the receiving Office or the International Searching Authority (Rule 46.2).

Where a demand for international preliminary examination has been/is filed, see below.

#### How?

Either by cancelling one or more entire claims, by adding one or more new claims or by amending the text of one or more of the claims as filed.

A replacement sheet must be submitted for each sheet of the claims which, on account of an amendment or amendments, differs from the sheet originally filed.

All the claims appearing on a replacement sheet must be numbered in Arabic numerals. Where a claim is cancelled, no renumbering of the other claims is required. In all cases where claims are renumbered, they must be renumbered consecutively (Administrative Instructions, Section 205(b)).

The amendments must be made in the language in which the international application is to be published.

#### What documents must/may accompany the amendments?

##### Letter (Section 205(b)):

The amendments must be submitted with a letter.

The letter will not be published with the international application and the amended claims. It should not be confused with the "Statement under Article 19(1)" (see below, under "Statement under Article 19(1)").

The letter must be in English or French, at the choice of the applicant. However, if the language of the international application is English, the letter must be in English; if the language of the international application is French, the letter must be in French.

## NOTES TO FORM PCT/ISA/220 (continued)

The letter must indicate the differences between the claims as filed and the claims as amended. It must, in particular, indicate, in connection with each claim appearing in the international application (it being understood that identical indications concerning several claims may be grouped), whether

- (i) the claim is unchanged;
- (ii) the claim is cancelled;
- (iii) the claim is new;
- (iv) the claim replaces one or more claims as filed;
- (v) the claim is the result of the division of a claim as filed.

The following examples illustrate the manner in which amendments must be explained in the accompanying letter:

1. [Where originally there were 48 claims and after amendment of some claims there are 51]:  
"Claims 1 to 29, 31, 32, 34, 35, 37 to 48 replaced by amended claims bearing the same numbers; claims 30, 33 and 36 unchanged; new claims 49 to 51 added."
2. [Where originally there were 15 claims and after amendment of all claims there are 11]:  
"Claims 1 to 15 replaced by amended claims 1 to 11."
3. [Where originally there were 14 claims and the amendments consist in cancelling some claims and in adding new claims]:  
"Claims 1 to 6 and 14 unchanged; claims 7 to 13 cancelled; new claims 15, 16 and 17 added." or  
"Claims 7 to 13 cancelled; new claims 15, 16 and 17 added; all other claims unchanged."
4. [Where various kinds of amendments are made]:  
"Claims 1-10 unchanged; claims 11 to 13, 18 and 19 cancelled; claims 14, 15 and 16 replaced by amended claim 14; claim 17 subdivided into amended claims 15, 16 and 17; new claims 20 and 21 added."

### "Statement under article 19(1)" (Rule 46.4)

The amendments may be accompanied by a statement explaining the amendments and indicating any impact that such amendments might have on the description and the drawings (which cannot be amended under Article 19(1)).

The statement will be published with the international application and the amended claims.

**It must be in the language in which the international application is to be published.**

It must be brief, not exceeding 500 words if in English or if translated into English.

It should not be confused with and does not replace the letter indicating the differences between the claims as filed and as amended. It must be filed on a separate sheet and must be identified as such by a heading, preferably by using the words "Statement under Article 19(1)."

It may not contain any disparaging comments on the international search report or the relevance of citations contained in that report. Reference to citations, relevant to a given claim, contained in the international search report may be made only in connection with an amendment of that claim.

### Consequence if a demand for international preliminary examination has already been filed

If, at the time of filing any amendments under Article 19, a demand for international preliminary examination has already been submitted, the applicant must preferably, at the same time of filing the amendments with the International Bureau, also file a copy of such amendments with the International Preliminary Examining Authority (see Rule 62.2(a), first sentence).

### Consequence with regard to translation of the international application for entry into the national phase

The applicant's attention is drawn to the fact that, where upon entry into the national phase, a translation of the claims as amended under Article 19 may have to be furnished to the designated/elected Offices, instead of, or in addition to, the translation of the claims as filed.

For further details on the requirements of each designated/elected Office, see Volume II of the PCT Applicant's Guide.

## PATENT COOPERATION TREATY

## PCT

## INTERNATIONAL SEARCH REPORT

(PCT Article 18 and Rules 43 and 44)

Applicant's or agent's file reference MEDY/P31555PC	<b>FOR FURTHER ACTION</b> see Form PCT/ISA/220 as well as, where applicable, item 5 below.	
International application No. PCT/GB2004/004060	International filing date (day/month/year) 27/09/2004	(Earliest) Priority Date (day/month/year) 27/09/2003
Applicant  MEDICAL RESEARCH COUNCIL		

This International Search Report has been prepared by this International Searching Authority and is transmitted to the applicant according to Article 18. A copy is being transmitted to the International Bureau.

This International Search Report consists of a total of 6 sheets.



It is also accompanied by a copy of each prior art document cited in this report.

1. Basis of the report

- a. With regard to the **language**, the international search was carried out on the basis of the international application in the language in which it was filed, unless otherwise indicated under this item.



The international search was carried out on the basis of a translation of the international application furnished to this Authority (Rule 23.1(b)).

- b. ☐ With regard to any **nucleotide and/or amino acid sequence** disclosed in the international application, see Box No. I.

2. ☒ **Certain claims were found unsearchable** (See Box II).

3. ☐ **Unity of invention is lacking** (see Box III).

4. With regard to the **title**,



the text is approved as submitted by the applicant.



the text has been established by this Authority to read as follows:

METHODS FOR IDENTIFYING COMPOUNDS INVOLVED IN THE PHOSPHOINOSITIDE-MEDIATED  
SIGNALLING AND USE THEREOF IN THE MANUFACTURE OF MEDICAMENTS

5. With regard to the **abstract**,



the text is approved as submitted by the applicant.



the text has been established, according to Rule 38.2(b), by this Authority as it appears in Box No. IV. The applicant may, within one month from the date of mailing of this international search report, submit comments to this Authority.

6. With regard to the **drawings**,

- a. the figure of the **drawings** to be published with the abstract is Figure No. 9



as suggested by the applicant.



as selected by this Authority, because the applicant failed to suggest a figure.



as selected by this Authority, because this figure better characterizes the invention.

- b. ☐ none of the figures is to be published with the abstract.

## INTERNATIONAL SEARCH REPORT

International Application No

PCT/GB2004/004060

## A. CLASSIFICATION OF SUBJECT MATTER

IPC 7 G01N33/50 A61P35/00 A61P9/10 A61P3/10 A61P25/00

According to International Patent Classification (IPC) or to both national classification and IPC

## B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)

IPC 7 G01N

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

Electronic data base consulted during the international search (name of data base and, where practical, search terms used)

EPO-Internal, PAJ, WPI Data, BIOSIS, EMBASE

## C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	<p>BOMPARD GUILLAUME ET AL: "Membrane targeting of protein tyrosine phosphatase PTPL1 through its FERM domain via binding to phosphatidylinositol 4,5-bisphosphate." JOURNAL OF CELL SCIENCE, vol. 116, no. 12, 15 June 2003 (2003-06-15), pages 2519-2530, XP002319141 ISSN: 0021-9533 abstract page 2524, column 2, line 16 - page 2526, column 1, line 26 Discussion</p> <p style="text-align: center;">----- -/--</p>	7,8,12, 13

☒ Further documents are listed in the continuation of box C.☒ Patent family members are listed in annex.

## \* Special categories of cited documents :

- \*A\* document defining the general state of the art which is not considered to be of particular relevance
- \*E\* earlier document but published on or after the international filing date
- \*L\* document which may throw doubts on priority claim(s) or which is cited to establish the publication date of another citation or other special reason (as specified)
- \*O\* document referring to an oral disclosure, use, exhibition or other means
- \*P\* document published prior to the international filing date but later than the priority date claimed

\*T\* later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention

\*X\* document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone

\*Y\* document of particular relevance; the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art.

\*G\* document member of the same patent family

Date of the actual completion of the international search

28 February 2005

Date of mailing of the international search report

14/03/2005

Name and mailing address of the ISA

European Patent Office, P.B. 5818 Patentlaan 2  
NL - 2280 HV Rijswijk  
Tel. (+31-70) 340-2040, Tx. 31 651 epo nl,  
Fax: (+31-70) 340-3016

Authorized officer

Vanhalst, K

## C.(Continuation) DOCUMENTS CONSIDERED TO BE RELEVANT

Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	WO 02/12276 A (MEDICAL RESEARCH COUNCIL; DOWLER, SIMON; CAMPBELL, DAVID; GRAY, ALEXAN) 14 February 2002 (2002-02-14) cited in the application abstract claims 1-4,11,13,19,43,46,47	14-17
A	US 5 821 075 A (GONEZ ET AL) 13 October 1998 (1998-10-13) abstract claims 1-12	1-6,9-11
A	WO 03/011901 A (UNIVERSITY OF DUNDEE; ALESSI, DARIO; VAN AALTEN, DAAN; THOMAS, CHRISTI) 13 February 2003 (2003-02-13) cited in the application abstract	1-17
T	KIMBER WENDY A ET AL: "Interaction of the protein tyrosine phosphatase PTPL1 with the PtdIns(3,4)P2-binding adaptor protein TAPP1." BIOCHEMICAL JOURNAL, vol. 376, no. 2, 1 December 2003 (2003-12-01), pages 525-535, XP002319142 ISSN: 0264-6021 the whole document	1-17
A	WO 01/57240 A (AGY THERAPEUTICS, INC; MELCHER, THORSTEN; KASK, KALEV) 9 August 2001 (2001-08-09) abstract	1-17
A	KIMBER W A ET AL: "Evidence that the tandem-pleckstrin-homology-domain-containi ng protein TAPP1 interacts with Ptd(3,4)P2 and the multi-PDZ-domain-containing protein MUPP1 in vivo" BIOCHEMICAL JOURNAL 01 FEB 2002 UNITED KINGDOM, vol. 361, no. 3, 1 February 2002 (2002-02-01), pages 525-536, XP001057247 ISSN: 0264-6021 abstract	1-17

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## C.(Continuation) DOCUMENTS CONSIDERED TO BE RELEVANT

Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
A	DOWLER S ET AL: "Identification of pleckstrin-homology-domain-containing proteins with novel phosphoinositide-binding specificities" BIOCHEMICAL JOURNAL 01 OCT 2000 UNITED KINGDOM, vol. 351, no. 1, 1 October 2000 (2000-10-01), pages 19-31, XP001096514 ISSN: 0264-6021 abstract	1-17
A	MARSHALL AARON J ET AL: "TAPP1 and TAPP2 are targets of phosphatidylinositol 3-kinase signaling in B cells: Sustained plasma membrane recruitment triggered by the B-cell antigen receptor" MOLECULAR AND CELLULAR BIOLOGY, vol. 22, no. 15, August 2002 (2002-08), pages 5479-5491, XP002319143 ISSN: 0270-7306 abstract	1-17

# INTERNATIONAL SEARCH REPORT

International application No.  
PCT/GB2004/004060

## Box II Observations where certain claims were found unsearchable (Continuation of item 2 of first sheet)

This International Search Report has not been established in respect of certain claims under Article 17(2)(a) for the following reasons:

1. ☒ Claims Nos.: 1-6, 8, 10, 12, 16, 17 (partially)  
because they relate to subject matter not required to be searched by this Authority, namely:  
Claims 4, 8, 10 and 12: Rule 39.1(iv) PCT - Diagnostic method practised on the human or animal body  
Claims 16 and 17: Rule 39.1(iv) PCT - Method for treatment of the human or animal body by therapy
2. ☐ Claims Nos.:  
because they relate to parts of the International Application that do not comply with the prescribed requirements to such an extent that no meaningful International Search can be carried out, specifically:
3. ☐ Claims Nos.:  
because they are dependent claims and are not drafted in accordance with the second and third sentences of Rule 6.4(a).

## Box III Observations where unity of invention is lacking (Continuation of item 3 of first sheet)

This International Searching Authority found multiple inventions in this international application, as follows:

1. ☐ As all required additional search fees were timely paid by the applicant, this International Search Report covers all searchable claims.
2. ☐ As all searchable claims could be searched without effort justifying an additional fee, this Authority did not invite payment of any additional fee.
3. ☐ As only some of the required additional search fees were timely paid by the applicant, this International Search Report covers only those claims for which fees were paid, specifically claims Nos.:
4. ☐ No required additional search fees were timely paid by the applicant. Consequently, this International Search Report is restricted to the invention first mentioned in the claims; it is covered by claims Nos.:

Remark on Protest

- ☐ The additional search fees were accompanied by the applicant's protest.  
☐ No protest accompanied the payment of additional search fees.



# INTERNATIONAL SEARCH REPORT

Information on patent family members

International Application No

PCT/GB2004/004060

Patent document cited in search report		Publication date	Patent family member(s)	Publication date
WO 0212276	A	14-02-2002	AU 7648801 A	18-02-2002
			EP 1385877 A2	04-02-2004
			WO 0212276 A2	14-02-2002
			US 2004106148 A1	03-06-2004
US 5821075	A	13-10-1998	AU 683299 B2	06-11-1997
			AU 7644394 A	22-03-1995
			CA 2170515 A1	09-03-1995
			EP 0789771 A2	20-08-1997
			JP 9510861 T	04-11-1997
			NZ 273219 A	26-06-1998
			WO 9506735 A2	09-03-1995
			US 6066472 A	23-05-2000
WO 03011901	A	13-02-2003	WO 03011901 A1	13-02-2003
			GB 2393725 A	07-04-2004
WO 0157240	A	09-08-2001	AU 3659101 A	14-08-2001
			CA 2398250 A1	09-08-2001
			EP 1255854 A2	13-11-2002
			JP 2003521247 T	15-07-2003
			WO 0157240 A2	09-08-2001
			US 2003092071 A1	15-05-2003
			US 2004072275 A1	15-04-2004
			US 2001049348 A1	06-12-2001

# PATENT COOPERATION TREATY

From the  
INTERNATIONAL SEARCHING AUTHORITY

# PCT

To:

see form PCT/ISA/220

## WRITTEN OPINION OF THE INTERNATIONAL SEARCHING AUTHORITY (PCT Rule 43bis.1)

Date of mailing  
(day/month/year) see form PCT/ISA/210 (second sheet)

Applicant's or agent's file reference  
see form PCT/ISA/220

**FOR FURTHER ACTION**  
See paragraph 2 below

International application No.  
PCT/GB2004/004060

International filing date (day/month/year)  
27.09.2004

Priority date (day/month/year)  
27.09.2003

International Patent Classification (IPC) or both national classification and IPC  
G01N33/50, A61P35/00, A61P9/10, A61P3/10, A61P25/00

Applicant  
MEDICAL RESEARCH COUNCIL

### 1. This opinion contains indications relating to the following items:

- ☒ Box No. I Basis of the opinion
- ☐ Box No. II Priority
- ☒ Box No. III Non-establishment of opinion with regard to novelty, inventive step and industrial applicability
- ☐ Box No. IV Lack of unity of invention
- ☒ Box No. V Reasoned statement under Rule 43bis.1(a)(i) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement
- ☐ Box No. VI Certain documents cited
- ☐ Box No. VII Certain defects in the international application
- ☐ Box No. VIII Certain observations on the international application

### 2. FURTHER ACTION

If a demand for international preliminary examination is made, this opinion will usually be considered to be a written opinion of the International Preliminary Examining Authority ("IPEA"). However, this does not apply where the applicant chooses an Authority other than this one to be the IPEA and the chosen IPEA has notified the International Bureau under Rule 66.1bis(b) that written opinions of this International Searching Authority will not be so considered.

If this opinion is, as provided above, considered to be a written opinion of the IPEA, the applicant is invited to submit to the IPEA a written reply together, where appropriate, with amendments, before the expiration of three months from the date of mailing of Form PCT/ISA/220 or before the expiration of 22 months from the priority date, whichever expires later.

For further options, see Form PCT/ISA/220.

### 3. For further details, see notes to Form PCT/ISA/220.

Name and mailing address of the ISA:



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WRITTEN OPINION OF THE  
INTERNATIONAL SEARCHING AUTHORITY

10/573508  
IAP9 Rec'd PCT/PTO 27 MAR 2006  
International application No.  
PCT/GB2004/004060

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Box No. I Basis of the opinion

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1. With regard to the **language**, this opinion has been established on the basis of the international application in the language in which it was filed, unless otherwise indicated under this item.
  - ☐ This opinion has been established on the basis of a translation from the original language into the following language , which is the language of a translation furnished for the purposes of international search (under Rules 12.3 and 23.1(b)).
2. With regard to any **nucleotide and/or amino acid sequence** disclosed in the international application and necessary to the claimed invention, this opinion has been established on the basis of:
  - a. type of material:
    - ☐ a sequence listing
    - ☐ table(s) related to the sequence listing
  - b. format of material:
    - ☐ in written format
    - ☐ in computer readable form
  - c. time of filing/furnishing:
    - ☐ contained in the international application as filed.
    - ☐ filed together with the international application in computer readable form.
    - ☐ furnished subsequently to this Authority for the purposes of search.
3. ☐ In addition, in the case that more than one version or copy of a sequence listing and/or table relating thereto has been filed or furnished, the required statements that the information in the subsequent or additional copies is identical to that in the application as filed or does not go beyond the application as filed, as appropriate, were furnished.
4. Additional comments:

**Box No. III Non-establishment of opinion with regard to novelty, inventive step and industrial applicability**

The questions whether the claimed invention appears to be novel, to involve an inventive step (to be non obvious), or to be industrially applicable have not been examined in respect of:

- ☐ the entire international application,  
☒ claims Nos. 1-6,8,10,12,14-17 (partially)

because:

- ☒ the said international application, or the said claims Nos. 1-6,8,10,12,16,17 (partially) relate to the following subject matter which does not require an international preliminary examination (*specify*):

**see separate sheet**

- ☒ the description, claims or drawings (*indicate particular elements below*) or said claims Nos. 14,15 (partially) are so unclear that no meaningful opinion could be formed (*specify*):

**see separate sheet**

- ☐ the claims, or said claims Nos. are so inadequately supported by the description that no meaningful opinion could be formed.  
☐ no international search report has been established for the whole application or for said claims Nos.  
☐ the nucleotide and/or amino acid sequence listing does not comply with the standard provided for in Annex C of the Administrative Instructions in that:

the written form

- ☐ has not been furnished  
☐ does not comply with the standard

the computer readable form

- ☐ has not been furnished  
☐ does not comply with the standard

- ☐ the tables related to the nucleotide and/or amino acid sequence listing, if in computer readable form only, do not comply with the technical requirements provided for in Annex C-bis of the Administrative Instructions.  
☐ See separate sheet for further details

**WRITTEN OPINION OF THE  
INTERNATIONAL SEARCHING AUTHORITY**

International application No.  
PCT/GB2004/004060

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**Box No. V Reasoned statement under Rule 43bis.1(a)(i) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement**

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1. Statement

Novelty (N)	Yes: Claims	1-6,9-11
	No: Claims	7,8,12-17
Inventive step (IS)	Yes: Claims	1-6,9-11
	No: Claims	7,8,12-17
Industrial applicability (IA)	Yes: Claims	7,9,11,13-15
	No: Claims	1-6,8,10,12,16,17

2. Citations and explanations

**see separate sheet**

**Re Item III**

**Non-establishment of opinion with regard to novelty, inventive step and industrial applicability**

- 1 In accordance with Rule 66.1(e) PCT, the written opinion with regard to novelty, inventive step and industrial applicability is restricted to the subject-matter that was searched, as outlined below:
  - 1.1 The subject-matter of claims 4,8,10 and 12 partially relates to methods of treatment, performed on the human or animal body and is therefore considered by this search authority to be covered by the provisions of Rule 67(iv) PCT. The Search has been restricted to those parts of the subject-matter relating to in-vitro methods.
  - 1.2 The subject-matter of claims 16 and 17 relates to methods of treatment, performed on the human or animal body and is therefore considered by this search authority to be covered by the provisions of Rule 67(iv) PCT. The search has been limited to the alleged effects of the compounds used.
  - 1.3 Present claims 14 and 15 relate to a compound defined by reference to a desirable characteristic or property, namely being able to modulate the interaction between PIP2 and TAPP. The claims cover all compounds having this characteristic or property, whereas the application provides support within the meaning of Article 6 PCT and disclosure within the meaning of Article 5 PCT for only a very limited number of such compounds. In the present case, the claims so lack support, and the application so lacks disclosure, that a meaningful search over the whole of the claimed scope is impossible. Independent of the above reasoning, the claims also lack clarity (Article 6 PCT). An attempt is made to define the compound by reference to a result to be achieved. Again, this lack of clarity in the present case is such as to render a meaningful search over the whole of the claimed scope impossible. Consequently, the search has been carried out for those parts of the claims which appear to be clear, supported and disclosed, namely those parts relating to the siRNA-compounds mentioned in the description at pages 56 and 62-63.

**Re Item V**

**Reasoned statement with regard to novelty, inventive step or industrial applicability;  
citations and explanations supporting such statement**

**1 Cited documents**

1.1 Reference is made to the following documents, the numbering will be adhered to throughout the examination procedure.

**D1:** BOMPARD GUILLAUME ET AL: "Membrane targeting of protein tyrosine phosphatase PTPL1 through its FERM domain via binding to phosphatidylinositol 4,5-biphosphate." JOURNAL OF CELL SCIENCE, vol. 116, no. 12, 15 June 2003 (2003-06-15), pages 2519-2530, XP002319141 ISSN: 0021-9533

**D2:** WO 02/12276 A (MEDICAL RESEARCH COUNCIL; DOWLER, SIMON; CAMPBELL, DAVID; GRAY, ALEXAN) 14 February 2002 (2002-02-14)

**D3:** US-A-5 821 075 (GONEZ ET AL) 13 October 1998 (1998-10-13)

**2 Novelty (Art. 33(2) PCT)**

2.1 None of the cited documents disclose the combination of features as stated in independent claims 1, 9, 10. The subject-matter of claims 1, 9, 10 and their dependent claims 2-6 and 11 is therefore new and fulfils the requirements of Article 33(2) PCT.

2.2 D1 discloses (the references in parentheses refer to this document):

2.2.1 A method for selecting a compound for modulating signalling via PIP2, comprising the step of identifying a compound (e.g. neomycin on p2526, col.1, lines 1-26) that modulates the intracellular localisation of PTPL1, as in claim 7, and exposing the PTPL1 polypeptide to the compound, as in claims 8, 12 and 13

2.3 D2 discloses (the references in parentheses refer to this document):

2.3.1 A compound that inhibits the interaction of PIP2 with TAPP (abstract; claim 19) and its use in the manufacture of a medicament for treatments of e.g. diabetes or ischaemic disease, cancer or inflammation disorders (abstract; claims 46 and 47), as in claims 14-17.

2.3.2 The siRNA molecule developed on the TAPP-1 sequence as described on p56 of the present application is however new, but cannot render the whole scope of the claims new.

2.4 The subject-matter of claims 7,8,12-17 is not new and the application does therefore not fulfil the requirements of Article 33(2) PCT.

### **3 Inventive step (Art. 33(3) PCT)**

3.1 D3 discloses (abstract; claims 1-12) a method for identifying compounds for modulating the cellular activity or location of PTPL1, from which the subject-matter of claim 1 differs in that the binding properties or cellular localisation of TAPP are analysed. It is at present not clear whether this difference in analysis method could result in an unexpected technical effect.

3.1.1 The objective problem can therefore be regarded as "How to provide an alternative method for identifying compounds for modulating the cellular activity or location of PTPL1?", the solution being the analysis of the binding properties or cellular localisation of TAPP.

3.1.2 D3 discloses (abstract; claims 1-12) a method that is largely similar to the one claimed in the present application, analysing the PTPL1 directly instead of looking at the TAPP protein and its effect on the PTPL1 pathway. The use of TAPP can therefore be seen as a selection out of several members of the PTPL1 pathway. However, since the present application is the first to report on the existence of a functional interaction between TAPP and PTPL1, it can not be assumed that the person skilled in the art would consider the use of the



TAPP protein in the method of D1. The choice of TAPP protein is therefore not obvious and involves inventive skills.

3.1.3 The subject-matter of claim 1 and its dependent claims 2-6, can therefore be considered to have an inventive step and fulfils the requirements of Article 33(3) PCT.

3.1.4 The same reasoning can be repeated for claims 9-11, because they are all founded on the functional relationship between PTPL1 and TAPP, unknown in the prior art.

3.1.5 Claims 9-11 are therefore inventive and fulfil the requirements of Article 33(3) PCT.

#### **4 Industrial applicability (Art. 33(4) PCT)**

4.1 The subject-matter of claims 1-6,8,10,12,16 and 17 (partially) relates to methods of treatment, performed on the human or animal body and is therefore considered by this search authority to be covered by the provisions of Rule 67(iv) PCT. Since there is no consensus between the different International Search Authorities on the possible patentability of such subject-matter, no opinion on industrial applicability of these claims can be given.

4.2 The remaining claims 7,9,11,13-15 are industrially applicable and fulfil the requirements of Article 33(4) PCT.